REMARKS

This Response is submitted in reply to the Office Action mailed August 26, 2003 ("the Action"). A Request for Continued Examination under 37 CFR 1.114 is submitted with this Amendment. Claims 1-42 are pending in the application but stand rejected under one or more of §112 and §103. Applicants will address the objections and rejections in the order raised in the Action below.

Interview

Applicant wishes to thank Examiner Jan Ludlow for the telephone interview with Applicant's attorney, Julie H. Richardson, on November 20, 2003. In the telephone interview, the Examiner agreed that proposed amendments to the claims resolve the outstanding §112 issues. In addition, the participants discussed the lack of motivation to combine the cited art references in view of the structure of the system of Sakazume. Examiner Ludlow agreed to consider this argument further upon receipt of the Amendment. A copy of the Applicant Initiated Interview Request Form, updated to note the discussion is attached.

Allowed Claims

Applicants acknowledge with appreciation the Examiner's allowance of Claims 32, 34-39 and 41-42.

Claim 32

Applicants have corrected the informality noted in Claim 32 and submit that it is allowed in its present form (as noted above).

§112, First Paragraph

The Action rejects Claims 17-21, 25, 27, 29, 31, 33 and 40 as failing to comply with the written description requirement because these claims recite "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention." More particularly, the Examiner opines that there was "no teaching with regard to": (a) the dispersing of clots formed prior to introduction into the containers; (b) movement distance relative to magnet/container spacing; and (c) moving containers along a continuous path." Applicants respectfully disagree.

In order to advance prosecution, Applicants have canceled Claims 33 and 40, which were directed to the "continuous path" feature (feature (c) above). However, Applicants believe that this operation would be readily understood as being one possible embodiment of the invention and such a feature is not excluded by certain of the pending claims.

Regarding the dispersion of clots (clotted magnetic particles in the fluid in the containers), Applicants note that certain embodiments of the present invention are directed to a starting point using a "clot" of magnetic particles (*see, e.g.*, page 3, lines 9-13 and page 4, lines 30-32 in support thereof). Indeed, the specification states: "It has been found that this results in a very efficient way of mixing the particles with the fluid, even when the particles as such tend to form a clot or had already formed a clot within the fluid." Emphasis added, page 4, lines 30-32. Claims 17 and 23 have been amended to more clearly correspond to this description (and Claims 18 and 24 depend therefrom). Accordingly, Applicants respectfully request that this rejection be withdrawn.

Regarding the movement/spacing rejection of Claims 19-22, 25, 27, 29 and 31, Applicants respectfully submit that the figures and specification support the recited features. For example, Claim 19 states that magnets in each array move forward and rearward in concert "so that adjacent arrays of magnets move in concert in opposing directions on opposite sides of a respective container array." At page 4, the specification states that when the container is placed between two magnets that strongly repel each other, the slightest movement of either one of the magnets or of the container with respect to each other will result in sudden strong changes of the magnetic field. The magnets may be placed in line so that each magnet repels each of its neighboring magnets. As stated in the application, the magnets may be placed in line in such a way that magnets of opposite polarities can be moved back and forth on

straight parallel paths along opposite sites of each container in such a way that the direction of the magnetic field in each container is repeatedly reversed. This may advantageously be achieved by placing the magnets in line in such a way that all magnets that are in line have their poles oriented in the same direction, and that all magnets in a neighboring line, that is on the other side of the containers next to the first line of magnets have their poles oriented in the reverse direction with respect to the pole of the magnets in the first line (p. 4, lines 35-45; p. 5 lines 1-5).

At page 5, the specification goes on to state that the magnets and container may be placed in parallel rows and the rows of magnets can be moved in opposite directions alongside the rows of containers. "But of course, based on the basic concept of the method of the invention other geometries can likewise be devised" (p. 5, lines 1-5).

Thus, Applicants respectfully submit that the subject matter is supported by the application. However, in order to advance prosecution, the objected to claims have been amended in a non-narrowing way to more clearly correspond with the written description.

The Cited Prior Art

The Action rejects the pending claims (except for allowed Claims 32, 34-39 and 41-42) over primary reference U.S. Patent No. 5,770,461 to Sakazume et al. ("Sakazume") in view of WO 96/26011 to Kirchanski et al. ("Kirchanski") or other secondary references. Applicants respectfully disagree.

In response to Applicants' pointing out that Sakazume teaches single magnets on either side of a container, the Examiner conceded in the Action (p. 6, para. 31) that "claims 1 and 16 recite plural arrays of magnets, but does not require each array to have plural magnets," thereby finding that an array could be a "1x1" array. Applicants have amended independent Claims 1 and 16 to recite that the magnet arrays comprise a plurality of spaced apart magnets. Sakazume fails to teach or suggest the subject matter recited in Claims 1, 6 and 16.

Further, Applicants respectfully submit that Sakazume does not teach a method and apparatus for immunoassays by mixing particles in containers using

magnets. Rather, Sakazume specifically states that, "by action of the permanent magnets, the magnetic micro particles are repetitively magnetically displaced or rotated to form flocks" (col. 9, lines 21-23, and col. 3, lines 3-15). Further, assuming, *arguendo*, that one could interpret the "repetitively magnetically displaced or rotated to form flock" operation to be a form of "mixing" according to the definition of mixing provided by the instant application, Sakazume itself contradicts this position. Sakazume states, "This agitation [due to the movement of the reaction container as described at Col. 5, lines 16-23] causes the washing liquid to be sufficiently mixed with the magnetic micro particles **20** as solid supports to disperse the particles which have been flocculated by a magnetic action, so as to sufficiently elude into the washing liquid substances adsorbed on the magnetic micro particles **20** as solid supports not by an immunological specific binding but in an unspecific manner" (col. 5, lines 23-28).

Thus, Sakazume teaches that sufficient mixing of the washing liquid with the magnetic micro particles can be achieved by mechanical means and, in addition, teaches away from the use of magnetic means for this purpose since they are causing flocculation, which has to be counteracted in an additional mechanical mixing step in order to achieve the required mixing. In addition, Sakazume clearly fails to teach or suggest magnet arrays comprising a plurality of spaced apart magnets that move in concert as well as other geometric and operational features recited in certain of the dependent claims above.

Kirchanski fails to resolve the deficiencies of Sakazume. Kirchanski states at page 3, lines 7-14, that:

> The magnetic separation process typically involves mixing the sample with paramagnetic particles in a liquid medium to bind the target substance by affinity reaction, and then separating the bound particle/target complex from the sample medium by applying a magnetic field. All magnetic particles except those that are colloidal settle in time. The liquid medium, therefore, must be agitated to some degree to keep the particles suspended for a sufficient period of time to allow the bioaffinity binding reaction to occur.

Thus, a goal of Kirchanski is to prevent sedimentation of the suspended particles without excess turbulence in the liquid. *See also*, page 5, lines 30-32. Further, as

conceded by the Action at page 6, para. 32, Kirchanski fails to teach or suggest magnet arrays, much less moving intervening magnet array geometries, with a plurality of magnet arrays as recited in independent Claims 1, 6, 16, 29 and 30. However, the Action then states that Sakazume teaches such a plurality of magnet arrays with a container array.

Notably, however, neither Sakazume or Kirchanski teach moving magnets in the magnet arrays (Claims 1 and 16) and/or oscillating the containers in the container array(s) about the magnet arrays to carry out the mixing (Claim 1 and other claims). Indeed, the magnets of Sakazume are stationary and the containers continuously advance past the magnet arrays (Figure 1). Kirchanski fails to teach or suggest magnet arrays. Contrary to the Action's statement otherwise, it is unclear to Applicants how one of skill in the art would have modified the configuration of Sakazume based on Kirchanski to arrive at the claimed invention absent the teachings of the present invention itself due, *inter alia*, to the structural constraints dictated by the system design of Sakazume (*see, e.g.*, Figure 1). Indeed, as noted in the prior response, both Sakazume and Kirchanski describe alternate magnetic embodiments but fail to teach or suggest the claimed configurations. Kirchanski fails to teach positioning a container array between two magnet arrays, much less cooperably moving magnet arrays to mix the fluid in the containers. Sakazume fails to teach or suggest moving magnets at all.

Applicants respectfully submit that there is no motivation to move the magnets in the static spaced apart magnet configurations proposed by Sakazume, as the magnets are configured as a subset of an overall system (*see* Figure 1, with the magnets positioned at location "E" per col. 5, lines 50-55). It is unclear how moving magnet arrays would be configured to fit within the proximately located upstream and downstream stations "D" and "E" *et seq.* (which provide technical and spatial constraints as well as operational requirements) of Sakazume. For example, how far would one move such magnets and magnet arrays when they are within the confines of the apparatus proposed by Sakazume to achieve the desired mixing? If the magnet arrays moved, how would they fit or operate with the units/components located upstream and downstream thereof (as fluctuating magnet fields would be produced).

Further, if the containers do not advance (*i.e.*, oscillate) how would they move to station "F" to carry out the next operation? In addition, if the containers of Sakazume were to oscillate, how far would they move to do so with respect to the upstream and downstream stations and what happens to the downstream and upstream container fluid (those not at the magnet station "E") as those containers would be repeatedly exposed to one or more upstream or downstream workstations? Thus, Applicants respectfully submit that there would have been no motivation for one of skill in the art to modify the static magnet station of Sakazume to use moving magnet arrays as claimed.

Although selected features of the claimed invention are found in the cited art references, the cited art references fail to teach or suggest the combination of the elements as claimed. Absent the teachings of the present invention, one of skill in the art would not have combined these references (as there is not motivation to do so) in a manner that would yield the claimed invention. It is improper to combine the separate elements of prior art references based on the teachings of the instant invention. In view of the foregoing, Applicants respectfully submit that one of skill in the art would not find the claimed invention obvious based on the combination of Sakazume and Kirchanski.

The dependent claims recited independently patentable subject matter such as, but not limited to, that the magnets in the magnet arrays and/or the containers in the container arrays move in concert (claims 4, 5, 6, 20, 25, 26 29, 30), that the magnets and/or containers move about straight and/or parallel paths (claims 10, 19, 21, 25, 29, 30), that the containers oscillate (claims 2, 20, 22, 26, 28), that adjacent arrays move in opposite directions (claims 21, 27), and the like.

New Claims

New dependent Claims 43 and 44 have been added to depend from Claim 30 in order to form a more complete claim set.

Conclusion

Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any matters outstanding of resolution, she is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

Respectfully submitted,

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CERTIFICATION OF FACSIMILE TRANSMISSION UNDER 37 CFR 1.8

I hereby certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office, GAU #1743, AF via facsimile number (703) 872-9310 on November 21, 2003.

Rosa Lee Brinson